CLAIMS

What is claimed is:

1. A method for producing a recombinant adenovirus comprising a gene of interest, without the concomitant production of replication competent adenovirus through homologous recombination, said method comprising:

providing a cell, said cell harboring nucleic acid based on or derived from adenovirus;

transferring recombinant nucleic acid into said cell, said recombinant nucleic acid comprising:

another nucleic acid based on or derived from adenovirus, and further including at least one functional encapsidating signal, and at least one functional Inverted Terminal Repeat, said recombinant nucleic acid lacking overlapping sequences with the cellular nucleic acid leading to replication competent adenovirus;

culturing said cell; and

harvesting recombinant adenovirus produced from said cell.

2. The method according to claim 1 wherein said recombinant nucleic acid is in linear form and comprises functional Inverted Terminal Repeats at or near both termini.

3. The method according to claim 1 wherein said cell is a primary cell.

4. The method of claim 1 wherein said recombinant nucleic acid is DNA.

5. The method of claim 2 wherein said recombinant nucleic acid is DNA.

6. The method of claim 3 wherein said recombinant nucleic acid is DNA.

7. A method of producing, in a producer cell, a recombinant adenovirus comprising a gene of interest, without the concomitant production of replication competent adenovirus through homologous recombination, said method comprising:

culturing, in a suitable medium, a producer cell comprising one or more recombinant nucleic acid molecules having no overlapping sequences with respect to one another which would otherwise allow for homologous recombination leading to replication competent adenovirus, wherein said producer cell expresses at least adenoviral E1A region gene products; and harvesting recombinant adenovirus produced from said cell.

8. The method according to claim 7 wherein at least one or more of said recombinant nucleic acid molecules of said producer cell further comprises a marker gene.

9. The method according to claim 8 wherein said marker gene is under control of an E1A responsive promoter, said E1A being of an adenovirus of the family *Adenoviridae*.

10. A method of producing a recombinant adenovirus comprising a gene of interest, without the concomitant production of replication competent adenovirus through homologous recombination, said method comprising:

culturing a producer cell in a suitable medium and harvesting said adenovirus therefrom, wherein said producer cell comprises:

one or more recombinant nucleic acid molecules having no overlapping sequences with respect to one another which would otherwise allow for homologous recombination leading to replication competent adenovirus in said producer cell, and wherein said producer cell expresses adenoviral E1 and E2A region gene products; and

harvesting recombinant adenovirus produced from said producer cell.

11. A method according to claim 10 wherein said E2A region is under the control of an inducible promoter.

12. A method according to claim 10 wherein said E2A region is mutated so that at least one of its products is temperature sensitive.

13. A method according to claim 11 wherein said E2A region is mutated so that at least one of its products is temperature sensitive.

14. The method according to claim 7 wherein said producer cell is a diploid cell.

15. The method according to claim 10 wherein said producer cell is a diploid cell.

16. The method according to claim 11 wherein said producer cell is a diploid cell.

17. The method according to claim 7 wherein said producer cell is of non-human origin.

18. The method according to claim 10 wherein said producer cell is of non-human origin.

19. The method according to claim 11 wherein said producer cell is of non-human origin.

20. The method according to claim 14 wherein said producer cell is of monkey origin.

21. The method according to claim 15 wherein said producer cell is of monkey origin.

22. The method according to claim 16 wherein said producer cell is of monkey origin.

23. A method according to claim 7 wherein one or more of said recombinant nucleic acid molecule of said producer cell further has a mutated E2A region of an adenovirus of the family *Adenoviridae*.

24. A method according to claim 10 wherein one or more of said recombinant nucleic acid molecule of said producer cell further has a mutated E2A region of an adenovirus of the family *Adenoviridae*.

25. A method according to claim 11 wherein one or more of said recombinant nucleic acid molecule of said producer cell further has a mutated E2A region of an adenovirus of the family *Adenoviridae*.

26. A method of producing a recombinant adenovirus comprising a gene of interest, without the concomitant production of replication competent adenovirus through homologous recombination, said method comprising:

culturing a producer cell in a suitable medium, said producer cell comprising:

one or more recombinant nucleic acid molecules having no overlapping sequences with respect to one another which would otherwise allow for homologous recombination leading to replication competent adenovirus in said producer cell, said producer cell further expressing adenoviral E1 and E2A region gene products, wherein said E2A region is mutated so that at least one of its products is temperature sensitive; and

harvesting said recombinant adenovirus from said cell.

27. A method of producing a recombinant adenovirus comprising a gene of interest, without the concomitant production of replication competent adenovirus through homologous recombination, said method comprising:

culturing a producer cell in a suitable medium, said producer cell comprising:

one or more recombinant nucleic acid molecules having no overlapping sequences with respect to one another, and DNA sequences encoding the adenoviral E1A and E1B region gene products; and

harvesting recombinant adenovirus from said cell.

28. The method according to claim 27 wherein said recombinant nucleic acid molecule further comprises DNA sequences encoding adenoviral E2A region gene products.

29. The method according to claim 28 wherein one of said DNA sequences encoding the E2A region gene product is selected from the group consisting of a DNA sequence encoding the wild-type E2A region operably linked to an inducible promoter and a DNA sequence encoding a temperature sensitive 125 mutation.